Practitioner's Docket No. MPI1997-018CP1DV1

REMARKS

Claims 32-46 are pending. The claims have been properly numbered to correct the inadvertent misnumbering in the previous response (paper no. 13). Claims 32 and 38 are amended herein. No new matter is added by virtue of the amendments. See, e.g., page 51, line 34 of the specification as filed.

Claims 32-46 were rejected under 35 USC §101 and 35 USC §112 as drawn to an invention with no apparent or disclosed patentable utility. The Examiner asserts while the present application describes isolated DNA encoding a protein and the protein encoded thereby, the application does not disclose the biological role of the protein or its significance. The rejection is traversed.

As acknowledged by the Examiner, the instant application has provided a description of an isolated DNA encoding a protein and the protein encoded thereby. In addition, the specification sets forth use of the described compositions in methods for diagnostics and identification of therapeutics for disorders, including, for example, metabolic disorders. Applicants submit the utility of diagnostics and screening methods for identification of therapeutics is an accepted substantial and real world utility in the pharmaceutical industry. Utility of diagnostics and therapeutics is well established and evident by the numerous issued patents relating to subject matter comprising diagnostic and therapeutic applications. Applicants' assertion of utility is based, not only on the homology of the identified compositions, but in conjunction with scientific exemplification set forth in Example 9 demonstrating specific expression patterns. The Examiner focuses on the specific biological mechanism and significance as Applicant's requirement to satisfy the utility requirement. Applicants respectfully submit this focus is undue and improper. Still further, the Office recognizes that intermediate, or research tool utilities can and do satisfy the Utility requirement. For example MPEP 2107.01 section addressing research tools:

> *Some confusion can result when one attempts to label certain types of inventions as not being capable of having a specific and substantial utility based on the setting in which the invention is to be used. One example is inventions to be used in a research or laboratory setting. **Many research tools such as gas chromatographs, screening assays, and nucleotide sequencing techniques have a clear, specific and unquestionable utility (e.g., they are useful in analyzing compounds).***

The Examiner asserts the claimed invention is not supported by a well established, substantial and specific asserted utility, and require extensive experimentation and thus, credibility cannot be assessed. Examiner Murphy ref rences generally the Utility Examination Guidelines. Applicants respectfully point out that the holding of the rejection based on a lack of a well established utility is improper in th present instance.

Practitioner's Docket No. MPI1997-018CP1DV1

The Examiner is correct in stating a utility rejection is proper where there is no readily apparent well established utility. Applicants respectfully point out that such requirement is due when no asserted utility is provided in an application, and a well established utility is not easily recognized. However, this is not the proper standard in this case, as the present application clearly sets forth an asserted utility (namely, use of the claimed polypeptides in methods for diagnostics and identification of therapeutics for disorders, including, for example, metabolic disorders). The standard which should be applied in the present application, is where an Applicant has asserted a specific and substantial utility in the specification, however the Examiner fails to recognize the asserted utility in this instance. In such a case, MPEP 2107.01 states: "the second type of deficiency arises in the rare instance where an assertion of specific and substantial utility for the invention made by an applicant is not credible."

Applicants again submit respectfully the threshold of the utility requirement which the Examiner sets forth in the present instance is improper and a rebuttal of the asserted utility has not been effectively made in the present case. The steps which should be taken in order to make a rejection should fall under MPEP 2107 (II)(C), where the Examiner is required to make a proper *prima facie* showing of no specific and substantial credible utility. See MPEP 2107(II)(C) (emphasis added):

> *(1) Where the asserted utility is not specific or substantial, a prima facie showing* ***must establish that it is more likely than not*** *that a person of ordinary skill in the art would not consider that any utility asserted by the applicant would be specific and substantial. The prima facie* ***showing must contain the following elements****:*
>
> *(i) An explanation that clearly sets forth the reasoning used in concluding that the asserted utility for the claimed invention is not both specific and substantial nor well-established;*
>
> *(ii)* ***Support for factual findings*** *relied upon in reaching this conclusion; and*
>
> *(iii) An evaluation of* ***all relevant evidence of record****, including utilities taught in the closest prior art.*

Applicants submit the Examiner has not made a sufficient showing to establish more likely than not the utility set forth in the present specification would not be specific or substantial, as sufficient support or factual findings have not been relied upon to make such a showing to rebut Applicant's assertion that the use in diagnostics and/or identification of therapeutics would more likely than not be useful. The Examiner makes a generic statement as to disbelief of the asserted utility because the molecule is a GPCR. However, this is not sufficient to meet the requisite standard that it is more likely than not that one of skill in the art would doubt Applicant's asserted utility. Applicants submit the Examiner has not made a sufficient showing to establish more likely than not the utility set forth in the present specification would not be specific or substantial, as sufficient support or factual findings have not been relied upon to

make such a showing to rebut Applicant's assertion that the use in diagnostics and/or identification of therapeutics would more likely than not be useful. Rather, the Examiner relies on general arguments to back up his claim that Applicant's original assertion is incorrect.

Applicants submit this is not the proper standard to maintain a utility rejection. In fact, this is counter to the guidance of the Office. According to the procedural considerations set forth in the MPEP 2107.02:

> *Thus, Langer and subsequent cases direct the Office to presume that a statement of utility made by an applicant is true. See In re Langer, 503 F.2d at 1391, 183 USPQ at 297; In re Malachowski, 530 F.2d 1402, 1404, 189 USPQ 432, 435 (CCPA 1976); In re Brana, 51 F.3d 1560, 34 USPQ2d 1436 (Fed. Cir. 1995). For obvious reasons of efficiency and in deference to an applicant's understanding of his or her invention, when a statement of utility is evaluated, Office personnel should not begin by questioning the truth of the statement of utility. Instead, any inquiry must start by asking if there is any reason to question the truth of the statement of utility. This can be done by simply evaluating the logic of the statements made, taking into consideration any evidence cited by the applicant. If the asserted utility is credible (i.e., believable based on the record or the nature of the invention), a rejection based on "lack of utility" is not appropriate. Clearly,* ***Office personnel should not begin an evaluation of utility by assuming that an asserted utility is likely to be false, based on the technical field of the invention or for other general reasons.***

Applicants submitted an independent publication and the corresponding PCT publication (English abstract submitted) of a separate group identifying I5E as a G protein coupled receptor and cognate ligands. The publications support Applicants' original assertion of I5E being a G-protein coupled receptor useful in identification of compounds capable of modulating I5E which can be useful for treating, for example digestive disorders. See, e.g., International publication no: WO02/062996 abstract. The Examiner, however, disregarded the submissions outright, because the information was not known at the filing date of Applicants' application. The Examiner argues the publications do not effectively rebut the rejection. However, Applicants again respectfully would like to point out that the submissions were made solely as support for Applicants' original assertions relating to the function of I5E. Since the Examiner has not yet met the requisite standard to reject the originally asserted utility, Applicants submit the Examiner's rejection of the references and associated arguments is moot. However, in an effort to clarify the submission, Applicants submit the publications and associated discussi n was made in an effort to point out to the Examiner that Applicants initial assertion is supported in fact by later studies of independent groups, further supporting the fact that Applicant's initial assertion is a specific substantial,

real world utility, and counter to any idea that one would find it is more likely than not that the initial assertion was not a specific substantial utility.

Additionally, the Examiner's rebuttal based on the lack of sufficient experimentation to establish beyond a reasonable doubt that administration of compounds would result in efficacy, etc. is improper. Applicants submit the utility set forth for the claimed subject matter of the present application is use in diagnostics and identification of therapeutics. The examiner's requirement that use of compounds for treatment would demonstrate efficacy is beyond the requisite standard. In fact, the requisite standard does not require Applicants provide evidence sufficient to establish that an asserted utility is true "beyond a reasonable doubt," or as a matter of statistical certainty, as the Examiner is seemingly requiring in the present case. *In re Irons*, 340 F.2d 974, 978, 144 USPQ 351, 354 (CCPA 1965); *Nelson v. Bowler*, 626 F.2d 853, 856-57, 206 USPQ 881, 883-84 (CCPA 1980). Rather a sufficient showing is made if, when considered as a whole, it leads a person of ordinary skill in the art to conclude that the asserted utility is more likely than not true. Applicants submit such standard has been met.

Thus, Applicants submit the utility asserted in the specification as filed is sufficient to support a credible, substantial, and specific utility to meet the requisite standard for utility under the present guidelines of the USPTO that the presently claimed compositions are useful in the identification of diagnostics and methods for identification of therapeutics for metabolic diseases. The Examiner has not yet made a sufficient showing to uphold a proper rejection of the claims under the utility requirement. Applicants thus respectfully submit the Examiner's maintenance of the rejection under 35 USC §101 and §112 are improper and should be withdrawn. Such action is respectfully requested.

Claims 32-46 were rejected under 35 USC 112, first paragraph, as not enabling one of skill in the art to use the invention commensurate in scope with the claims because "the specification does not disclose the nexus between the I5E polypeptide and an immune, central nervous system or metabolic disorder, cognitive disorder, multiple sclerosis or depression..."

Applicants respectfully traverse the rejection, and submit the breadth of the claims is not undue in view of Applicant's specification as filed and the skill of one in the art. Applicants again respectfully point out to the examiner that the present claims are not limited to methods of treatment of particular indications, but rather are directed to methods for identification of compounds which modulate I5E. Applicants have in fact provided sufficient disclosure of the sequences and methods in order to carry out the present claims. The Examiner's attention is directed, for example to section 5.4 of the application at pag s 28-52, containing full description of the compositions and methods for use in practicing the present claims. The Examiner is again held to the idea that the claims are not nabled because a definitive in vivo clinical proof of a nexus betwe n I5E activity and/or expression and disease state has not been shown.

Practitioner's Docket No. MPI1997-018CP1DV1

Applicants further submit the language of the claims would be well understood to those of skill in the art as to the claimed methods of screening compounds to identify modulators of I5E as *candidate* compounds capable of treating disease. It is well understood in the industry that the process of therapeutic drug development is a long process, of which the screening of compounds is at the beginning, though crucial and valuable step. It is well understood that compounds identified in such screens may ultimately not be therapeutically effective, albeit for various reasons. However, the fact remains, the screening process is a valuable method in the early stages of the drug development process.

Applicants submit the claims would be well understood to one of skill in the art, and are fully enabled. However, in an effort to clarify, Applicants have amended claims 32 and 38 to address any concerns of the Examiner. Support for the amendments lies in the specification as filed (see, e.g., page 51, line 34). Reconsideration and withdrawal of the rejection is thus respectfully requested.

This paper is being filed timely, and it is believed no fees or extensions of time are required in connection with the present submission. In the event any additional extensions of time are necessary, the undersigned hereby authorizes the requisite fees to be charged to Deposit Account No. 501668.

Entry of the remarks made herein is respectfully requested. It is believed the application is presently in a state for immediate allowance, which action is earnestly solicited.

Respectfully submitted,

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